REMARKS

Status of application

Applicants note that this application has been pending since December 13, 1996, which is more than five years. In accordance with MPEP § 707.02, "[a]ny application that has been pending five years should be carefully studied by the supervisory patent examiner and every effort made to terminate its prosecution. In order to accomplish this result, the application is to be considered "special" by the examiner."

Status of the claims

Claims 1-12, 14-59, 62-88 are pending in the present application. Claims 1-5, 20-37, 39-40, 42-43, and 46-56 were previously withdrawn from consideration as drawn to a non-elected invention. Claims 13, 60, and 61 were previously canceled. By virtue of this response, claims 7-10, 12, and 64 have been canceled, claims 6, 11, 14, 15, 65, 71, and 82-88 have been amended, and new claims 89-99 have been added. Accordingly, claims 6, 11, 14-19, 38, 41, 44, 45, 57-59, 62-63, and 65-99 are currently under consideration.

The claim amendments and new claims are supported by the specification, for example, on page 30, line 1 - page 32, line 29, and on page 53, lines 21-22. No new matter has been added by the foregoing amendments.

With respect to all amendments and canceled claims, Applicants have not dedicated to the public or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to

pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional applications.

Telephone interview

Applicants wish to thank Examiners Rawlings and Caputa for extending the courtesy of a telephone interview on May 7, 2003. Applicants appreciate the Examiners' helpful suggestions, which are reflected in this response. Applicants have given careful consideration to the issues raised in the outstanding Office Action and in the telephone interview and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Claim objection

Claim 59 is objected to as reciting a polynucleotide encoding both the light and heavy chain variable region sequences contained in SEQ ID NOs: 2 and 4, respectively, whereas claim 6, upon which claim 59 depends, recites a polynucleotide encoding a polypeptide comprising the light *or* heavy chain CDRs. The Examiner states that "a polypeptide of claim 6 cannot have both the light and heavy chain variable region sequences of the monoclonal antibody 11D10, as required by claim 59, because claim 6 requires the polypeptide to comprise one or the other, *not both*."

Claim 6 as amended is directed to a polynucleotide that encodes a polypeptide comprising both light and heavy chain CDR's, rendering this objection moot. However, Applicants note that the term "comprises" as used in claim 6 prior to the current amendment and in new claim 90 is a term of art that permits additional unrecited elements to be included within the scope of a claim. Use of this term with respect to the present claims permits inclusion of sequences other than those which are specifically recited. MPEP § 2111.03. The term "or" does not exclude other sequences from the claim. The three CDRs of the light chain *or* the heavy chain must be comprised (*i.e.*

included) within the claimed polypeptide encoded by the claimed polynucleotide, but other sequences may be included as well, in view of the term "comprises."

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the objection to claim 59.

Rejection under 35 U.S.C. § 101

Claims 14, 15, and 82-88 are rejected under 35 U.S.C. § 101 as allegedly not supported by either a specific and substantial asserted utility, a credible asserted utility, or a well-established utility. Applicants respectfully traverse this rejection.

During the telephone interview of May 7, 2003, Examiner Caputa stated that since the claimed polynucleotides encode 11D10 sequences, a disclosed use of these polynucleotides for recombinant production of 11D10 polypeptides would be sufficient to establish utility under 35 U.S.C. § 101.

As discussed in the response filed on September 26, 2002, and in the telephone interview of May 7, 2003, the specification discloses several specific, substantial, credible, and well-established utilities for the claimed polynucleotides. For example, the specification discloses use of the claimed polynucleotides for recombinant production of antibody 11D10 polypeptides, as primers for amplification of 11D10 sequences, and as probes for detection of the presence of 11D10 polynucleotides in a cell. All of these utilities represent well-established uses for polynucleotides. Each of these uses is specific, since the claimed polynucleotides require specifically disclosed polynucleotides sequences that encode 11D10 polypeptides. Each of these uses is also substantial because use of polynucleotides as probes, primers, or in recombinant production systems are "real world" uses that do not require further research by a person of skill in the art. A person of skill in the art would also consider any of these uses credible, and the Examiner has not provided any evidence to the contrary.

During the telephone interview of May 7, 2003, Examiner Caputa stated that since the claimed polynucleotides encode 11D10 sequences, a disclosed use of these polynucleotides for recombinant production of 11D10 polypeptides would be sufficient to establish utility under 35 U.S.C. § 101. As discussed in the response filed on September 26, 2002, disclosure supporting use of the claimed polynucleotides in a recombinant expression system may be found, for example, on page 37, lines 15-19, of the specification. Further disclosure may be found, for example, on page 47, lines 1-20. The Examiner's statement that "any small or large part of a nucleic acid molecule encoding an antibody might be used to construct a recombinant version of an antibody" (Office Action, sentence bridging bottom of page 3 and top of page 4) indicates that this use is well-established. Further, this use is specific, because expression is directed to defined, disclosed sequences, substantial, because the claimed polynucleotides encode useful polypeptides, namely 11D10 polypeptides (including 11D10 antibody and fragments thereof) or useful recombinant forms of 11D10, and credible, because recombinant methods and use of recombinant expression systems are routine in the art.

In order to satisfy the statutory requirement for utility, Applicants need to provide only one credible assertion of specific and substantial utility. MPEP § 2107. As discussed above, Applicants have disclosed several specific, substantial, and credible utilities that are well-established uses for polynucleotides, including recombinant production of 11D10 polypeptides, which Examiner Caputa stated in the telephone interview would be sufficient to establish utility. Therefore, the presently-claimed invention satisfies the utility requirement for patentability.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Rejection under 35 U.S.C. § 112, first paragraph

Enablement rejections

Claims 14, 15, and 82-88 are rejected as allegedly lacking enablement since the claimed invention is allegedly not supported by a specific and substantial, credible, or well established utility. Applicants respectfully traverse this rejection.

During the telephone interview of May 7, 2003, Examiner Caputa stated that disclosure of recombinant production of 11D10 polypeptides would be sufficient to satisfy the utility requirement. As discussed above, this use is disclosed in the specification. Therefore, since the claimed invention is supported by a utility, as discussed in the interview, this enablement rejection should be withdrawn.

As discussed above, the invention is supported by a number of specific, substantial, and credible utilities, including recombinant production of 11D10 polypeptides. One of skill in the art would readily understand how to make and use polynucleotides in a recombinant expression system without undue experimentation, since such techniques are routine in the art. Therefore, the claimed invention is enabled by the specification, which discloses use of the claimed polynucleotides to recombinantly produce 11D10 polypeptides, as discussed above.

The Examiner states that "the asserted utility lacks credibility, because the art suggests the claimed invention could not be used to elicit the required immune response and the use of the claimed invention to elicit the immune response has not been exemplified." The Examiner does not state to which "art" he is referring. Further, "exemplification" is not the standard for utility, but rather whether an asserted utility is specific, substantial, and credible, or well established, from the standpoint of a person of skill in the art. Therefore, it is not necessary for Applicants to exemplify use of the claimed invention to elicit an immune response in order for the invention to satisfy the enablement requirement. As discussed above, Applicants have asserted several utilities for the claimed polynucleotides in addition to use for eliciting an anti-HMFG immune response, including uses as probes, primers, and for recombinant production of 11D10 polynucleotides. As noted above, in the recent telephone interview, Examiner Caputa stated that disclosure of recombinant production of 11D10 polypeptides was sufficient to satisfy the utility requirement. Since Applicants have disclosed such a utility, this enablement rejection should be withdrawn, as discussed during the interview.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 6-12, 16-19, 38, 41, 44, 45, 59, 62-64, 66, 70, 71, and 76-81 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled for a polynucleotide sequence encoding an immunoglobulin variable region containing the three light chain CDRs of antibody 11D10 *or* an immunoglobulin variable region containing the three heavy chain CDRs of antibody 11D10, wherein said polynucleotide encodes a polypeptide capable of eliciting an anti-HMFG immunological response in a mammal. Applicants respectfully traverse this rejection.

Solely to expedite prosecution, claim 6 has been amended to recite a polynucleotide encoding an immunoglobulin variable region containing the three light chain CDRs *and* the three heavy chain CDRs. During the telephone interview, the Examiners indicated that this would be sufficient to overcome the enablement rejection.

New claim 90 recites an isolated polynucleotide comprising the three light chain CDRs *or* the three heavy chain CDRs, without the functional language "capable of eliciting an anti-HMFG immunological response in a mammal." During the telephone interview of May 7, 2003, Examiner Caputa, who suggested this claim, stated that amending the claims in this way would be sufficient to abrogate the enablement rejection.

For completeness, Applicants provide the following response to statements made by the Examiner in the Office Action. The Examiner states that a skilled artisan would not have a reasonable expectation of success in making and using the claimed invention without undue experimentation. Applicants respectfully note that "reasonable expectation of success" is the standard for *obviousness*, not enablement. The standard for enablement is whether the specification provides *adequate guidance* such that the skilled artisan could make and use the invention without undue experimentation. As discussed in the response filed on September 26, 2002, the specification provides examples of methods for making the claimed polynucleotides (see, for example, page 33,

line 23 - page 34, line 6) according to methods that are well known in the art, *e.g.*, chemical synthesis, recombinant production, PCR amplification. The specification also provides examples of methods for testing and using the claimed polynucleotides to elicit an immune response (see, for example, page 48, line 33 - page 51, line 12, and page 90, line 31 - page 91, line 8), using assays that are routine in the art. Thus, the specification provides adequate guidance for making and using the claimed invention according to methods that are common to the art, enabling the claimed invention.

The Examiner also states that there is "factual evidence of record" that embodiments of the claimed invention could not be used to elicit an anti-HMFG immune response with a reasonable expectation of success without performing an undue amount of additional experimentation. The Examiner does not indicate what the "factual evidence of record" is that he is referring to. Further, as discussed above, "reasonable expectation of success" is the standard for obviousness, not enablement.

Applicants also note that claim 6 recites that the claimed polynucleotides encode a polypeptide that gives rise to an anti-HMFG response. Thus, the claim excludes these postulated inoperable embodiments. Finally, even if the claim did not recite this limitation, the mere possibility that some embodiments would not elicit an anti-HMFG response is insufficient grounds for alleged lack of enablement. The law of enablement clearly allows for inoperable embodiments. MPEP § 2164.08(b); *Atlas Powder Co. v. DuPont*, 750 F.2d 1569, 1576 (Fed. Cir. 1984).

The Examiner cites *Colbert v. Lofdahl*, 21 USPQ2d 1068, 1071 (BPAI 1992), in which the court stated that it is not sufficient to define a recombinant molecule by its principal biological activity in the context of the specificity required to show conception. The issue addressed in this case was conception, not enablement. Thus, *Colbert v. Lofdahl* is inapplicable to the claimed invention, and is an inappropriate citation for an enablement rejection.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 6-12, 16-19, 38, 41, 44, 45, 59, 62-71, and 76-81 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled for an isolated polypeptide that is "capable of" eliciting an anti-HMFG immune response in a mammal. The Examiner stated that amending claim 6 to recite that the claimed polynucleotide is capable of eliciting an anti-HMFG immunological response "upon administration to said mammal" would be sufficient to overcome the rejection. Solely to expedite prosecution, claim 6 has been so amended, rendering the rejection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Written description rejections

Claims 6-19, 38, 41, 44, 45, 57-59, 62, 63, 66, 70, and 72-88 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description for the genus claimed. Applicants respectfully traverse this rejection.

During the telephone interview of May 7, 2003, Examiner Caputa stated that structural information or identifying characteristics provide sufficient written description under 35 U.S.C. § 112, first paragraph. Examiner Caputa stated that claim 6 satisfies this standard and that a claim as reflected by new claim 90 would satisfy this standard. Applicants respectfully note that the specification provides structural information regarding the claimed invention in the form of polynucleotide and polypeptide sequences for antibody 11D10, and identifying characteristics in the form of the light and heavy chain CDRs. Therefore, the invention is supported by adequate written description.

Citing *The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement* (66 FR 1099-1111), the Examiner states that an adequate written description of the claimed invention must include sufficient description of at least a

representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicants were in possession of the claimed genus. In response, Applicants note that all of the claimed polynucleotides encode the CDR's of antibody 11D10. The CDR's are relevant identifying characteristics of this genus of polynucleotides. Sequences for the CDR's are provided in the specification. These sequences provide common structural information about the polynucleotides within the scope of the claims, showing that Applicants were in possession of the claimed genus at the time of filing.

The Examiner further states that for inventions in an "unpredictable" art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In response, Applicants note that MPEP § 2163(3)(a)(ii) states that "[w]hat constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the *necessary common attributes or features* of the elements possessed by the members of the genus in view of the species disclosed." (emphasis added) In the instant case, Applicants have provided sequences for the CDR's, which are the common features encoded by the claimed genus of polynucleotides. One of skill in the art would recognize that Applicants were in possession of these features from the description in the specification. This same section of the MPEP further states that "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, *but not necessarily any particular species*." (emphasis added) With respect to the present invention, Applicants have provided sufficient structural information, *e.g.*, sequences of the CDR's of antibody 11D10, such that one of skill in the art would accept that

Applicants were in possession of the full genus of polynucleotides claimed. Thus, the claimed invention is supported by adequate written description.

The Examiner states that "contrary to Applicants' assertion, the recitation of the limitation "isolated" does not exclude genomic polynucleotides from the claimed genus, even in view of the definition of the term "isolated," which is set forth in the specification." Applicants strongly traverse this statement. The definition for "isolated" which is set forth on page 16, lines 13-14 of the specification is *"substantially free of the materials with which it is associated in nature."* A polynucleotide which is substantially free of the materials with which it is associated in nature is separated from the genome from which it is derived. Applicants do not understand the relevance of the Examiner's statement, in view of the claimed invention.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 82-88 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description support. Applicants respectfully traverse this rejection.

The Examiner states that the specification does not appear to provide support for the recitation of "comprising a region of at least _____ contiguous nucleotides" in claims 82, 85, and 86 but that the specification provides support for "comprising a region of at least *about* _____ contiguous nucleotides" (emphasis added). During the telephone interview, Examiner Caputa agreed with Applicants' representative that there is support in the specification for the claims as written. However, in order to expedite prosecution, Applicants have amended the claims to recite "at least about," rendering the rejection moot. During the telephone interview, Examiner Caputa stated that the term "about" is acceptable claim language, as set forth in MPEP §2173.05(b).

The Examiner states that the specification does not provide support for the recitation of "comprising a region of at least ____ contiguous nucleotides" in claims 83, 84, 87, and 88.

Applicants respectfully note that support for these claims is provided on page 32, lines 9-19, of the specification.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 103(a)

Claims 6-12, 14-19, 38, 41, 44, 45, 57-59, 62-66, and 70-88 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Bhattacharya-Chatterjee et al., 1994, in *Antigen and Antibody Molecular Engineering in Breast Cancer Diagnosis and Treatment*, Ceriani, R.L., ed., Plenum Press, New York, pp. 139-148, in view of Chakraborty et al., *Proceedings of the American Association for Cancer Research*, 35:497, Abstract No. 2963, and further in view of Kennedy et al., 1985, *Biotechniques* 3:404-410, and WO 94/11508-A2 (May 26, 1994) or Spooner et al., 1995, *Gene Therapy* 2:173-180 and Stevenson et al., 1995, *Immunological Reviews* 145:211-228 and in still further view of Herlyn et al., 1995, *Hybridoma* 14:159-166. Applicants respectfully traverse this rejection.

During the telephone interview on May 7, 2003, Examiner Caputa stated that providing newly-executed declarations with typographical errors corrected, discussed below, would render the declarations sufficient to overcome all of the outstanding art rejections.

In response to Applicants' argument that neither the Bhattacharya-Chatterjee et al. reference nor the Chakraborty et al. reference is an enabling reference and that antibody 11D10 was not available to the public prior to filing of the application, as set forth in previously submitted declarations of the inventors under 37 C.F.R. §1.132, the Examiner reiterates his position that the declarations are insufficient, for reasons provided in the previous Office Action. The previously-submitted declarations of inventors Malaya Bhattacharya-Chatterjee and Sunil Chatterjee include a typographical error in a sentence declaring that to the best of their knowledge and belief, the public did not have access to the 11D10 cell line or antibody prior to filing of the application. Due to a

clerical error, the word "not" was omitted and the sentence reads "the public did have access." During the telephone interview on May 7, 2003, Examiner Caputa stated that providing newly-executed declarations with these typographical errors corrected would render the declarations sufficient to overcome all of the outstanding art rejections. New declarations, signed by Malaya Bhattacharya-Chatterjee and Sunil Chatterjee are submitted herewith as Exhibit A. Each of these declarations includes a corrected sentence in paragraph 8 that states that the public did *not* have access to the cell line or antibody prior to filing of the application.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 6-12, 14-19, 38, 41, 44, 45, 57-66, and 70-88 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chakraborty et al., 1995, *Cancer Research* 55:1525-1530, in view of Spooner et al., 1995, *Gene Therapy* 2:173-180, and Stevenson et al., 1995, *Immunological Reviews* 145:211-228, or Kennedy et al., 1985, *Biotechniques* 3:404-410, and WO 94/11508-A2 (May 26, 1994), and in further view of Herlyn et al., 1995, *Hybridoma* 14:159-166. Applicants respectfully traverse this rejection.

The Examiner states that Applicants have traversed this ground of rejection by submitting a declaration under 37 CFR § 1.132 by Malaya Bhattacharya-Chatterjee which states that Mala Chakraborty did not make any independent contributions to generating monoclonal antibody 11D10 and that Heinz Kohler did not participate in any way in the process of generating or characterizing the monoclonal antibody 11D10. This statement by the Examiner is incorrect. The declaration to which the Examiner refers was submitted with the response filed on September 26, 2002, to overcome a 35 U.S.C. § 102(a) rejection based on a *Journal of Immunotherapy* paper coauthored by Mala Chakraborty, not the *Cancer Research* paper which serves as a basis of the present §103(a) rejection. The *Cancer Research* paper was addressed in the declaration of Malaya Bhattacharya-Chatterjee originally submitted with the response filed on May 17, 1999, and resubmitted herewith in Exhibit A.

The Examiner states that the declaration by Malaya Bhattacharya-Chatterjee is insufficient, since it fails to apprise of the inventive roles or contributions of Sonjoy Mukerjee and Roberto Ceriani, coauthors of the *Cancer Research* paper. As discussed above, the Examiner is referring to the wrong declaration. The declaration of Malaya Bhattacharya-Chatterjee submitted on May 17, 1999, which is resubmitted herewith in Exhibit A, addresses the roles and contributions of Sonjoy Mukerjee and Roberto Ceriani.

Applicants respectfully reiterate their previous argument that the Chakraborty et al. *Cancer Research* paper is not available as prior art under §102(a), since it represents work that was done under the direction of the inventors and was published less than one year prior to the fling of the present application. Applicants note that this reference was cited and withdrawn as a § 102 reference in related application U.S. serial no. 08/766,350, which has the same priority date as the instant application. The roles and contributions of the authors of the Chakraborty et al. *Cancer Research* paper have been addressed in the declaration of Malaya Bhattacharya-Chatterjee, which is resubmitted in Exhibit A, discussed above. This declaration shows that the Chakraborty et al. reference is not available as a § 102(a) or § 102(f) reference, and since it was published less than one year prior to the filing date, it is also not available as a § 102(b) reference. Therefore, the Chakraborty et al. *Cancer Research* paper is not available as a supporting reference for a § 103(a) rejection since it is not a prior art reference under § 102.

As discussed above, the declarations of Malaya Bhattacharya-Chatterjee and Sunil Chatterjee which are submitted herewith in Exhibit A, have been amended to correct a typographical error and now state that "the public did not have access" to the 11D10 cell lines or antibodies prior to filing of the application. In the telephone interview on May 7, 2003, Examiner Caputa stated that this correction to the declarations would be sufficient to overcome all of the outstanding art rejections.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Double patenting

Claims 64, 65, and 71 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 12, 23, and 24 of U.S. Patent 6,274,143 in view of WO 94/11508. Applicants will address this issue upon obtaining otherwise allowable subject matter. The Examiner is invited to consider whether a two-way test should apply in view of the significant length of time this case has been pending in the Office.

Applicants also bring co-owned, copending patent application nos. 08/766,350 and 10/367,506 to the Examiner's attention. The present application is the subject of a double patenting rejection in copending application 08/766,350.

CONCLUSION

Applicants have, by way of the amendments and remarks presented herein, removed the issues for the rejections and addressed all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 304142000322.

Respectfully submitted,

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